Remarks

Claims 1-61 are currently pending in this application. Claims 5 and 56-59 are amended. Claim 5 has been amended to remove recitation of SEQ ID NOs: that are not part of the elected Group III, and claims 57 and 58 have been amended to no longer depend on withdrawn claims. Claim 11 has been canceled, and the limitations thereof have been added to claim 5. The amendments to claim 5 and cancellation of claim 11 have been made because Applicants noticed that claim10 did not further limit claim 5, and that claim 11 was broader in scope than claim 10. As it now stands, claim 5 is broader in scope than its dependent claim 10. As indicated in the Action, these amendments place claims 5, 57, and 58 in condition for allowance. Applicants note that the Action indicated claim 53 is allowable if rewritten in independent form, because it currently depends on rejected claim 46. However, Applicants have not amended claim 53, preferring to traverse the rejection of claim 46 at this time.

1. Claim Rejections - 35 USC §112, first paragraph, enablement

A. Claim 11 is rejected under 35 USC §112, first paragraph as not enabled for an antibody that is at least 90% identical to the sequence described in SEQ ID NOs: 16 and 18 (15C4) and that inhibits binding of either IL-1β or IL-1ra to IL-1R1. The Action indicated that amending the claim to recite "wherein the antibody inhibits binding of IL-1β to IL-1R1" would overcome the rejection. As discussed above, claim 11 has been canceled and, solely in order to expedite prosecution of the instant claims, claim 5 has been amended to include the suggested phrase "wherein the antibody inhibits binding of IL-1β to IL-1R1." Applicants, therefore, respectfully submit that the instant rejection has been overcome.

B. Claims 1, 2, 32-38, 40, 42, 44, 46-49, 52, and 53 stand rejected under 35 USC §112, as not enabled for antibodies that comprise less than the complete light and heavy chain variable domains. Specifically, the Action asserts that the specification does not provide objective evidence of any particular antibody variable domains that can bind to antigen on its own. The Action also states that "the instant specification does not provide sufficient guidance or direction to enable one of ordinary skill in the art, without undue experimentation, to make an antibody that specifically binds IL-1R1 starting with molecules comprising **a subset** of the six CDRs required for antibody binding."

This rejection relies on the teachings of Janeway *et al.* In particular, citing Janeway *et al.*, the Action states that "all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required confirmation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites." In addition, the Action states that Applicants have not provided objective evidence that any particular antibody variable region in the application can bind to antigen "in the absence of a complementary heavy or light chain variable region containing all three CDRs."

Applicants have reviewed the pages from Janeway *et al.* that were provided by the Office (pages 3:1-3:3), but cannot find any language that explicitly supports the Action's position with respect to CDRs. Furthermore, as discussed extensively in Applicants' Response to the previous Office Action and directly contrary to the interpretation in the Action to the asserted teachings of Janeway, one of skill in the art will recognize that antibodies do not necessarily have to have both the heavy and the light chain to bind an antigen as taught in US Patent No. 6,248,516 and Desmyter et al. (2001), J. Biol. Chem. 276(28): 26285-90 (cited in the prior response). For instance, Applicants respectfully point out that the Patent Office has recognized that antibodies can be claimed by identifying a single CDR domain (see, for example, US Patent Nos. 6,951,646; 6,914,128; 6,090,382; 6,818,216; 6,156,313; 6,827,925; 5,833,943; 5,762,905; and 5,760,185). Also, as discussed in the response to the previous Office Action, the CDR3 domains can determine binding specificity of an antibody (see discussion of Schier et al., 1996, J. Mol. Biol. 263: 551-67; and Desiderio et al., 2001, J. Mol. Biol. 310: 603-15 in the previous Response).

Applicants submit that the recitation of at least the CDR3 domains and/or at least one of the heavy or light chain variable regions, together with the limitation of binding to IL-1R1, should be sufficient to enable one of skill in the art to make and use the antibodies of the invention. However, Applicants have provided more than this, including, for example, the extensive discussion in the specification on page 33, line 16 to page 41, line 10.

Therefore, Applicants submit that the claims are enabled, and respectfully request that these grounds of rejection be withdrawn.

C. Claims 56 and 59 stand rejected as not enabled, because the claims encompass antibodies that bind the amino acid sequence YSV of IL-1R1. The Action specifically asserts

that the claim encompasses antibodies that can bind any YSV peptide and not just YSV in the context of IL-1R1. The claims as amended recite that the antibodies bind "to a region of IL-1R1 that comprises the amino acid sequence YSV." As mentioned previously, the specification provides exemplary antibodies whose binding to IL-1R1 is abolished when amino acids in binding site 4 (YSV) are changed (see Examples 5 and 9). The specification teaches methods (for example, on pages 33-48) and additional methods are known to those of skill in the art that can be used to generate antibodies using an antigen that comprises binding site 4 (YSV) of IL-1R1. Thus, claims 56 and 59 are enabled.

2. Claim Rejections - 35 USC §112, first paragraph, written description

A. Claims 1, 2, 32-38, 40, 42, 44, 46-49, 52, 53, 56, and 59 also stand rejected as not satisfying the written description requirement. Specifically, the Action asserts that one of skill in the art "cannot envision all the contemplated heavy and light chain possibilities recited in the instant claims..." and "have not demonstrated possession of a single species of antibody that can recognize isolated YSV polypeptide."

As discussed in the Response to the previous Office Action, those of skill in the art recognize that antibodies do not always require a light chain, a heavy chain, and all six CDRs from the light and heavy chains for binding specificity of an antibody to a particular epitope. A number of antibodies that bind IL-1R1 are described in the specification, including 15C4, 26F5, 27F2, 24E12, and 10H7. Applicants specifically describe the variable regions of these antibodies, the CDRs of these antibodies (see, for example, Figures 10 and 11), describe functional assays demonstrating activity of these antibodies (see, for example, Examples 3 and 4), and describe epitopes for these antibodies (see, for example, Examples 5 and 9). The claims encompass antibodies that comprise these heavy and light chain variable regions, antibodies that comprise CDR3 of both the heavy and light chains, and the claims require that the antibodies specifically bind to IL-1R1. Applicants respectfully submit that one of skill in the art will recognize that the claims are not drawn to antibodies that could also comprise *any* heavy or light chain variable region or *any* CDR, but only those heavy and light chain variable regions or CDRs that will still allow for binding to IL-1R1. The specification provides assays that will identify these antibodies.

Since the art of making antibodies is considered to be more mature, *i.e.*, more predictable,

than some other areas of biotechnology, and Applicants teach many particular sequences of IL-1R1 binding antibodies, one of skill in the art would conclude that Applicants were in possession of the common attributes of the claimed antibodies. Consequently, Applicants submit that the claims satisfy the written description requirement, and respectfully request that this ground of rejection be withdrawn.

Regarding claims 56 and 59, the claims as amended recite that the antibodies bind to a region of IL-1R1 that comprises the amino acid sequence YSV. Written description is satisfied where an applicant provides a functional characteristic of the invention and correlates the function with a structure. *Noelle v. Lederman* citing *Enzo Biochem v. Gen-Probe,* 323 F.3d 956, 964 (Fed. Cir. 2002). Applicants have provided the functional characteristic, binding to IL-1R1, and have correlated the function with a structure, the epitope being a portion of IL-1R1 that comprises YSV. Therefore, Applicants submit that claims 56 and 59 satisfy the written description requirement, and respectfully request that this ground of rejection be withdrawn.

B. Claim 11 is rejected under 35 USC §112, first paragraph as failing to comply with the written description requirement. Specifically, the Action asserts that Applicants have not provided support for an antibody with at least 90% identity to an antibody comprising SEQ ID NOs: 16 and 18 that inhibits binding of either IL-1β ***or IL-1ra*** to IL-1R1. As discussed above, this limitation in claim 11 is now recited in claim 5, but the phrase has been amended, as discussed above, to recite that the antibody inhibits binding of IL-1β to IL-1R1 as suggested in the Action. Therefore, Applicants submit that the amendment has overcome this ground of rejection.

3. Claim Rejections - 35 USC §102

Claims 55 and 56 stand rejected under 35 USC §102(e) as being anticipated by US Patent No. 6, 511, 665 (the '665 patent) as evidenced by Vigers *et al.* The Action asserts that the antibodies taught in the '665 patent "inherently contain antibodies that specifically bind to the polypeptide of SEQ ID NO: 76." The Action bases this position on the following: 1) "Dower teaches that human antibodies developed against the soluble truncated form of IL-1 receptor are particularly preferred"; 2) "antibodies against IL-1R1 may be utilized therapeutically to block the binding of IL-1 to its receptor"; and 3) "antibodies which specifically recognize the extracellular

domain of IL-1R1, in particular domain three of IL-1R1, would block binding of IL-1 to its receptor as evidenced by Vigers."

As noted in the Action, the '665 patent mentions that antibodies against the soluble truncated form of IL-1 receptor are preferred. However, the '665 patent does not mention the specific sequence described in SEQ ID NO: 76 as having any particular importance for making antibodies against the soluble form of IL-1 receptor, nor does the '665 patent actually disclose or make any of these preferred antibodies.

Furthermore, the Action asserts that the preferred antibodies mentioned in the '665 patent would specifically recognize domain three of IL-1R1, because Vigers *et al.* teach that "site B" of IL-1β contacts domain three. However, Vigers *et al.*, while teaching that "site B" binds to domain 3 of IL-1R1, never give the actual sequence of domain 3 or indicate in any other way that the sequence of SEQ ID NO: 76 is important for generating antibodies against IL-1R1.

Moreover, the Action presents an inherent anticipation argument. Inherency requires a showing in the cited reference that the feature in question would necessarily flow from the prior art. Since no antibodies made in the '665 patent were tested for the ability to block binding of IL-1 to its receptor, it is simply speculation that any such antibody would bind this portion of the receptor as presently claimed. The Action has failed to meet its burden of showing inherency and thus, the instant claims cannot be anticipated by the '665 patent even when taking the teachings of Vigers *et al.* into account under section 102. Consequently, Applicants respectfully request that this ground of rejection be withdrawn.

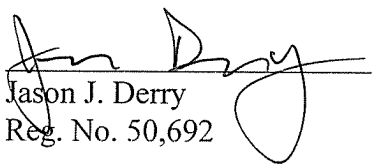
CONCLUSION

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended or as originally presented. Allowance of the claims is thereby respectfully solicited.

The Examiner in charge of this application is invited to contact the undersigned representative as indicated below if it is believed to be helpful.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff LLP

Date: December 8, 2006

By: 
Jason J. Derry
Reg. No. 50,692

Phone: 312-913-0001
Fax: 312-913-0002